REMARKS

Introductory Comments

Reconsideration of the above-identified application in view of the above amendments and foregoing arguments is respectfully requested.

Claims 52-61, 69 and 77-81 are pending and under consideration. Claims 62-68 and 70-76 have been canceled. Claims 55, 60, 69, 77, 80 and 81 have been amended. Specifically, claim 61 now recites "and degenerate codon equivalents thereof" from canceled claim 71 and claim 69 is now dependent on claim 57 since claim 67 is now canceled. The amendment to claim 77 is explained below. Additionally, claims 55, 60, 77, 80 and 81 have been amended in order to place the claims in a better form by specifying the sequence is an amino acid sequence. No new matter has been added as a result of these amendments.

Objection of Claims 62-68 and 72-76 Under 37 C.F.R. 1.75

Claims 62-68 and 72-76 are objected to under 37 C.F.R. 1.75 as being a substantial duplicate of claims 52-58. Applicants have canceled these claims and the objection is now moot.

Rejection of Claims 77-78 Under 35 U.S.C. § 112, Second Paragraph

Claims 77-78 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Specifically, the Examiner states that "at least one" in the preamble of claim 77 is unclear as a word appears to be missing. Applicants have amended claim 77 to recite "at least one antibody". This amendment is supported in the specification on page 9, lines 8-18. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 77-78 under 35 U.S.C. § 112, second paragraph.

Rejection of Claims 57-59, 61, 67-69, 71, 77-79 and 81 Under 35 U.S.C. § 112, First Paragraph

Claims 57-59, 61, 67-69, 71, 77-79 and 81 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply to the written description requirement, that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner states that the BS322 polypeptides of the claimed invention encompass proteins that are not adequately described in the specification as filed, since neither the claims nor the specification as filed indicate what distinguishing structural or functional attributes the members of the claimed genus of polypeptides share. The Examiner then states that the specification and claims do not place any limit on the number of amino acid substitutions, deletions and/or additions that may be made to the claimed polypeptides and it is only required that the BS322 polypeptides contain at least 50% identity to the polypeptide sequences according to SEQ ID NOS: 24-28. According to the Examiner, the scope of the claims therefore includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between the genus members are permitted. Applicants respectfully traverse the rejection.

The inquiry into whether the description requirement is met is determined on a case-by-case basis and is a question of fact. Section 2163 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003). When a question regarding the adequacy of the written description arises, the fundamental factual inquiry is whether the specification conveys to those skilled in the art, as of the filing date sought, that applicant was in possession of the invention being claimed. Section 2163.02 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003). Possession can be shown in a number of ways. For example, an Applicant can show possession by: (1) an actual reduction to practice of the claimed invention; (2) a clear depiction of the invention in detailed

drawings or in structural chemical formulas which permit a person skilled in the art to clearly recognize that applicant had possession of the claimed invention; or (3) any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Id.*

A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the Examiner to rebut the presumption. Section 2163.04 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003). The Examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. *Id.* The Examiner has the initial burden of presenting by a preponderance of the evidence why a person skilled in the art would not recognize in an applicants disclosure a description of the invention as defined by the claims. *Id.* "A general allegation of unpredictability in the art is not a sufficient reason to support a rejection for lack of adequate written description." *Id.* The *Manual of Patent Examining Procedure* even cautions Examiners that "rejection of an original claim for lack of written description should be rare." (See Section 2163 *Manual of Patent Examining Procedure* (8th Edition, Rev. 1, Feb. 2003)).

The U.S. PTO has issued Guidelines governing its internal practice for assessing whether the specification contains an adequate written description of the invention being claimed. In its Guidelines, the PTO has determined that the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics..., i.e., the complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, January, 2001 *Guidelines*, 66 Fed. Reg. at 1106.

Contrary to the arguments made by the Examiner, Applicants submit that the specification adequately describes the polypeptides encompassed within the scope of the invention being claimed. First, as specifically recommended by the

Guidelines, Applicants have provided the complete structure of the claimed polypeptides as demonstrated in SEQ ID NOS: 24-28. Second, with respect to the issue raised by the Examiner regarding the "numerous structural variants" and the "number of amino acid substitutions, deletions and/or additions that may be made to the claimed polypeptides", Applicants submit that because the level of skill in the area of molecular biology is considerably high, one of ordinary skill in the art, after reviewing Applicants specification, would clearly recognize that the Applicants have provide an adequate written description of the variants, substitutions, deletions and/or additions encompassed by the claims. Applicants specifically direct the Examiner's attention to page 30, lines 21-32 of the specification where it states that "Thus a polypeptide of the present invention may have an amino acid sequence that is identical to that of the naturally occurring polypeptide or that is different by minor variations due to one or more amino acid substitutions. The variation may be a "conservative change" typically in the range of about 1 to 5 amino acids, wherein the substituted amino acid has similar structural or chemical properties, e.g., replacement of leucine with isoleucine or threonine with serine. In contrast, variations may include nonconservative changes, e.g., replacement of a glycine with a tryptophan. Similar minor variations may also include amino acid deletions or insertions, or both. Guidance in determining which and how many amino acid residues may be substituted, inserted or deleted without changing biological or immunological activity may be found using computer programs well known in the art, for example, DNASTAR software (DNASTAR Inc., Madison, WI)." As illustrated by the above cited portion of the specification, computer programs are available to those of ordinary skill in the art and these programs can be used in providing guidance in determining "which and how" many amino acids residues in SEQ ID NOS: 24-28 can be substituted, inserted or deleted. Use of such programs are well known to those of ordinary skill in the art.

Therefore, in view of the aforementioned arguments, Applicants submit that one of ordinary skill in the art would clearly recognize that Applicants had possession of the claimed invention and have provided an adequate written

description. Thereupon, Applicants respectfully submit that the Examiner has failed to provide sufficient factual evidence to rebut the presumption that the description as filed is inadequate. Moreover, the Examiner fails to present any factual evidence as to why a person of ordinary skilled in the art would not recognize in Applicants disclosure a description of the invention as defined by the claims. In view of the absence of such evidence, Applicants submit that this rejection should be withdrawn.

Rejection of 52-61, 70 and 77-81 Under 35 U.S.C. § 101 and § 112, First Paragraph

The Examiner maintains the rejection of claims 52-61, 70 and 77-81 under 35 U.S.C. § 101 and § 112, first paragraph, as applied in the previous Office Action.

The rejection applying 35 U.S.C. § 112, first paragraph, has been addressed above. Applicants' arguments above are incorporated herein.

With respect to the rejection under 35 U.S.C. § 101, the Examiner contends that Applicants' arguments using the Jager *et al.* reference in the previous Response is not persuasive.

Firstly, the Examiner states that contrary to Applicants' assertion, it is noted that Jager *et al.* describe the identification of two NY-BR-1 splice variants (page 2058 and Figure 3), wherein the two sequences differ only by the presence of an additional coding sequence of 111 bp in one splice variant, and is absent in the other variant. The Examiner concludes that there is no evidence of an additional splice variant that produces polypeptides according to SEQ ID NOS: 24-28 of the instant invention.

Secondly, the Examiner states that Applicants consistently refer to the similarity between the polynucleotide sequences of BS322 consensus sequence (SEQ ID NO: 9) and NY-BR-1, but the instant claims are drawn to the polypeptides according to SEQ ID NOS: 24-28 instead. According to the Examiner, Applicants have not provided any objective evidence that would demonstrate that the individual peptides according to SEQ ID NOS: 24-28

represent actual NY-BR-1 antigen epitopes such that antibodies targeting these peptides could be potentially useful in detecting diseases of the breast or used in a method for treating breast cancer. The Examiner notes that the Jager *et al.* reference states that antibody probes must be produced in order to confirm breast specificity of NY-BR-1 at the protein and cell levels (page 2059, second column, second paragraph). Citing two references, the Examiner concludes that Applicants have not provided evidence that the relative mRNA abundance of BS322 transcript encoded by SEQ ID NO: 9, in breast tissue would be predictative of the corresponding relative abundance of the BS322 polypeptides in breast tissue. Applicants respectfully traverse the rejection based on these reasons.

Firstly, it is unclear as to the Examiner's basis of the rejection by stating that Jager *et al.* disclose two splice variants of NY-BR-1. The fact that both of these splice variants are highly similar (the only difference is 111 bp as pointed out by the Examiner), would indicate that the difference between both variants are not significant. Applicants are not required to show that the claimed polypeptides are derived from both variants, if both variants are linked to breast diseases. Nevertheless, Applicants are required only to show that the claimed polypeptides are derived from one polynucleotide which is linked to breast disease. This information was provided in the previous Response, showing the 100% alignment match between NY-BR-1 and SEQ ID NO: 9, excluding the exons (See page 3 of Applicants' previous Response and Exhibit A). Applicants' arguments presented in the previous Response are incorporated herein. As to the derivation of the polypeptides from SEQ ID NO: 9, Applicants' disclosure clearly states that the polypeptides are derived from SEQ ID NO: 9. Page 49, lines 5-12 clearly states that SEQ ID NO: 9 is the consensus sequence of SEQ ID NOS: 1-6. Page 64, lines 3-32 clearly describes how SEQ ID NOS: 24-28 are derived from translation of open reading frames of SEQ ID NO: 9. Therefore, Applicants submit that the specification clearly show how SEQ ID NOS: 24-28 are derived from a polypeptide that is shown to be linked to breast disease in

view of the Jager *et al.* reference. Methods for translation of polypeptides from polynucleotides are well known to one of ordinary skill in the art.

Secondly, with respect to the Examiner's contention that Applicants have not provided any objective evidence that would demonstrate that the individual peptides according to SEQ ID NOS: 24-28 represent actual NY-BR-1 antigen epitopes such that antibodies targeting these peptides could be potentially useful in detecting diseases of the breast or used in a method for treating breast cancer, Applicants would like to point out the following.

As disclosed in the specification, the claimed polypeptides contain epitopes that are relevant to the binding of substrates and therefore useful as markers for other molecules. Such features are not describable in terms in words. On page 20, lines 5-10, it is disclosed the significance of an epitope, which is defined as an antigenic determinant of a polypeptide or protein, and the method of determining such is by spatial confirmation (x-ray crystallography or two dimensional nuclear magnetic resonance) which are known to those of ordinary skill in the art. On page 20, lines 11-15, it is described that a conformation epitope, as well known in the art, is comprised of a specific juxtaposition of amino acids in an immunologically recognizable structure, such amino acids being present on the same polypeptide in a contiguous or non-contiguous order. Thus, the description of the epitopes, a structural feature of the claimed polypeptides, is not easily describable by words. Therefore, the significance of the structure of the polypeptides are described via their SEQ ID NO as allowed in the Eli Lilly cases discussed in the USPTO Written Description Guidelines.

The Examiner's attention is also directed to *Noelle v. Lederman* (69 USPQ2d 1481 (CAFC 2004)) where the Court held that a claim directed to an antibody which is capable of binding to a particular antigen has sufficient support in the written description that discloses "fully characterized" antigens. The Court stated that if an applicant has disclosed fully characterized antigens, either by structure, formula, chemical name, physical properties, or by deposit in a public

depository, then the applicant can claim the antibody by its affinity to the described antigen.

Applicants' disclosure describes methods such as complex formation of immunogenic specific binding members using the claimed polypeptides for detecting breast diseases (page 23, line 7 to page 26, line 10). Additionally, Applicants' specification discloses the exact sequence containing the exact amino acids of the claimed polypeptides, SEQ ID NOS: 24-28. This equates to the structure, formula and chemical name as discussed in *Noelle*. *Noelle* held that the affinity of the antigen to the antibody is significant and cannot be ignored.

With respect to the Examiner's citation of the Jager *et al.* passages and two additional articles conferring to the concept that antibody probes must be produced in order to confirm breast specificity of NY-BR-1 at the protein and cell levels (page 2059, second column, second paragraph) and that relative mRNA abundance of BS322 transcript encoded by SEQ ID NO: 9, in breast tissue would not be predictative of the corresponding relative abundance of the BS322 polypeptides in breast tissue, Applicants would like to make the following points.

The specification does not indicate anywhere that the use of the claimed polypeptides require an abundance of relative mRNA of BS322 transcript encoded by SEQ ID NO: 9. In fact, the claims are drawn to a polypeptides and methods of using the polypeptides for detecting antibodies specific for the BS322 antigen. The claims <u>are not drawn to a method of directly curing diseases</u> of the breast although the claimed methods of detection of antibodies ultimately can be useful in treating diseases of the breast.

Accordingly, Applicants respectfully request withdrawal of the rejection of claims 52-61, 70 and 77-81 under 35 U.S.C. § 101.

CONCLUSION

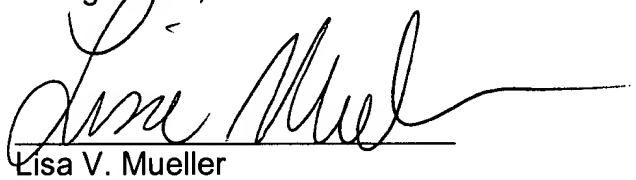
Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. Sections 101 and 112. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Should the Examiner have any questions concerning the above, she is respectfully requested to contact the undersigned at the telephone number listed below. If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

If any additional fees are incurred as a result of the filing of this paper, authorization is given to charge deposit account no. 23-0785.

Respectfully submitted,

Billing-Medel, *et al.*



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